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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/691,383	10/17/2000	Edwin F. Ullman	BEH-7381	3713

34500 7590 11/13/2003

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EXAMINER	
COOK, LISA V	

ART UNIT	PAPER NUMBER
1641	10

DATE MAILED: 11/13/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No. 09/691,383	Applicant(s) ULLMAN ET AL.	
	Examiner Lisa V. Cook	Art Unit 1641	

--Th MAILING DATE of this communication appears on the cov r sheet with th correspond nc address --

THE REPLY FILED 10 September 2003 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.

b) ☒ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.
ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2. ☐ The proposed amendment(s) will not be entered because:

   (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);

   (b) ☐ they raise the issue of new matter (see Note below);

   (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

   (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____.

3. ☐ Applicant's reply has overcome the following rejection(s): _____.

4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5. ☒ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *See attached.*

6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7. ☒ For purposes of Appeal, the proposed amendment(s) a)☐ will not be entered or b)☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

   The status of the claim(s) is (or will be) as follows:

   Claim(s) allowed: *NONE.*

   Claim(s) objected to: *NONE.*

   Claim(s) rejected: *19-34.*

   Claim(s) withdrawn from consideration: *NONE.*

8. ☐ The proposed drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9. ☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.

10. ☐ Other: _____

LONG V. LE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600
11/06/03

Lisa V. Cook 1st 10/14/03
11/3/03

ADVISORY ACTION

Amendment Entry

1. Applicant's response to the Final Office Action mailed 14 July 2003 is acknowledged (Paper No.9 filed 9/10/03). In amendment-B filed therein claims 1-18 were cancelled without prejudice or disclaimer. Currently, claims 19-34 are under consideration.

OBJECTIONS WITHDRAWN

Information Disclosure Statement

2. The listing of references in the specification is not a proper information disclosure statement. For example see page 12. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the examiner-on form PTO-892 or the applicant-on form PTO-1449 have cited the references they have not been considered.

3. The information disclosure statement (IDS) filed 3/6/091 in paper #2 has been considered as to the merits before First Action.

Applicants contend that all relevant references have been included in the IDS filed in paper #. Accordingly the objection is withdrawn.

REJECTIONS MAINTAINED

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

I. Claims 19-20 and 23-26 are rejected under 35 U.S.C. 102(b) as being anticipated by Oh et al. (US Patent #5,851,778) or Oh et al. (WO 89/03041).

In both the cited references Oh et al. employ a conjugate that comprises three moieties or members to evaluate specific binding partners. Two members of the conjugate are relatively small molecules (lees than about 7,000 Daltons). When the conjugate is bound by a macromolecular specific binding partner (sample drug –analyte), it sterically inhibits the binding of other/different macromolecules to another member of the three-member conjugate. See abstract of both references.

An assay protocol is outlined in figure 1 of both references. Therein an assay employing a tridentate complex (1st reagent) comprising biotin (first label), 1st hapten (drug analog), and 2nd hapten (small molecule) is mixed with a sample (free analyte – first hapten/drug), avidin (second label), antibody to the first hapten (antibody to the drug), and an antibody to the second hapten (antibody to the small molecule).

Examples of small molecule members are listed on page 29 – 1st paragraph (WO 89/03041) and column 13 line 65 through column 14 line 12 (US Patent #5,851,778). This list includes drugs, biotin, and dyes as recite in claim 20. The binding interaction is evaluated using proximity labels (page 35 WO 89/0304 – column 16 US Patent 5,851,778), enzymes (page 36 WO 89/03041- column 17 US Patent #5,851,778), or donor-acceptor pairs (page 37 WO 89/03041 – column 18 US Patent#5,851,778).

Both references evaluate the signal from the target molecules as an increase over background or control signals (predetermined signals). See example 5 through example 7 (column 34 –column 39 US Patent #5,851,778 and pages 73-83 of WO 89/03041).

Response to Argument

Applicant argues that although Oh et al. teach a tridentate conjugate equivalent to the instantly claimed first reagent, it does not anticipate the instant invention because it dos not teach the utility of multiple reagents. Specifically indicating that Oh et al. do not teach multiple antibodies. This argument was carefully considered but not found persuasive because Oh et al. teach the utility of two antibodies (multiples) in their assay design in figure 1. In figure 1 of both patents an antibody to the first hapten and an antibody to a second hapten are employed.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., multiple drug detection with multiple antibodies) are not recited in the rejected claim(s). It is noted that the instant claims read on not just multiple drug detection but also single drug detection (one or more drugs in a sample).

Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

With respect to the assay being utilized to measure more than one analyte with multiple reagents (tridentate conjugates) it is noted that even though every limitation of a claimed process is not disclosed in the prior art reference, anticipation can be found on the inferences which one skilled in the art would reasonably expect to draw therefrom. *In re Preda* (CCPA 1968) 401 F2d 825, 159 USPQ 342. Further Oh et al. teach that other drugs can be effectively assayed in competition by their method in column 16 lines 30-49(5,851,778) and page 34 (WO 89/03041).

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negative by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

II. Claims 21 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Oh et al. (US Patent #5,851,778) or Oh et al. (WO 89/03041) in view of Maggio (Immunoenzyme technique I, CRC press © 1980, pages 186-187).

Oh et al. (US Patent #5,851,778) or Oh et al. (WO 89/03041) are set forth above.

Oh et al. (US Patent #5,851,778) or Oh et al. (WO 89/03041) differ from the instant invention in not specifically teaching the detection assay employing a solid phase such as particles.

However, Maggio disclose enzyme immunoassays wherein either the antigen or antibody is immobilized onto a solid phase. The solid phase can be particles, cellulose, polyacrylamide, agarose, discs, tubes, beads, or micro plates (micro titer plates). See page 186.

Oh et al. (US Patent #5,851,778) or Oh et al. (WO 89/03041) and Maggio are analogous art because they are from the same field of endeavor, all the inventions teach methods involving immunoassays.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use solid phase/particles as taught by Maggio in the assay method to detection the drugs interaction of Oh et al. (US Patent #5,851,778) or Oh et al. (WO 89/03041) because Maggio taught that solid phase assay systems employing particles/microplates/discs/tubes/beads "are very convenient to wash thereby reducing labor in assay procedures". Please see page 186.

III. Claims 27-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Oh et al. (US Patent #5,851,778) or Oh et al. (WO 89/03041) in view of Zuk et al. (U.S.Patent#4,281,061).

The teachings of Oh et al. (US Patent #5,851,778) or Oh et al. (WO 89/03041) are set forth above. However, these references fail to teach the assay as a kit.

Zuk et al. (4,281,061) teach that "as a matter of convenience the reagents [of an immunoassay] can be provided as kits, where the reagents are in predetermined ratios, so as to substantially optimize the sensitivity of the assay in the range of interest" (column 22, lines 63-66).

It would have been prima facie obvious to one of ordinary skill in the art at the time of applicant's invention to take the detection assay as taught by Oh et al. (US Patent #5,851,778) or Oh et al. (WO 89/03041) because Zuk et al. teach that it is convenient to do so and one can enhance sensitivity of a method by providing reagents as a kit. Further, the reagents in a kit are available in pre-measured amounts, which eliminates the variability that can occur when performing the assay. Although the reference does not specifically disclose that a kit would have instructions which teach how to use said kit, it would have been prima facie obvious to any one of ordinary skill in the art to include instructions which describe how to perform the assay. Applicants should note that the printed matter on the instructions in a kit cannot serve to define the kit over the prior art. See in re Gulack 217 USPQ (CAFC 1983).

Response to Arguments

6. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Namely applicant contends that the Maggio and Zuk do not teach the claimed assay procedure. It is noted that the references were cited in combination with Oh et al. wherein Oh et al. teach the claimed process.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, Maggio taught that solid phase assay systems employing particles, microplates., discs, tubes, or beads "are very convenient to wash thereby reducing labor in assay procedures".

While, Zuk et al. teach that it is convenient to format reagents as kits and one can enhance sensitivity of a method by providing reagents as a kit.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., multiple drug detection with multiple antibodies) are not recited in the rejected claim(s). It is noted that the instant claims read on not just multiple drug detection but also single drug detection (one or more drugs in a sample). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

7. For reasons aforementioned, no claims are allowed.

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION REMAINS FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Remarks

9. Prior art made of record and not relied upon is considered pertinent to the applicant's disclosure:

A. Lehnen (U.S. Patent #5,567,627) teach methods and reagents useful in the simultaneous and discrete analysis of multiple analytes.

B. Terstappen et al. (U.S. Patent #5,646,001) affinity-binding separation and release of one or more selected subset of biological entities from a mixed population thereof.

10. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Group 1641 Fax number is (703) 872-9306, which is able to receive transmissions 24 hours/day, 7 days/week.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa V. Cook whose telephone number is (703) 305-0808. The examiner can normally be reached on Monday-Friday from 8:00 AM - 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, can be reached on (703) 305-3399.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Lisa V. Cook
CM1-7B17
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10/14/03
Lisa V. Cook